UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/071,541	05/04/1998	H.-J. SU HUANG	28685	5607

7590 06/30/2005

MARTIN D. MOYNIHAN
C/O ANTHONY CASTORINA
2001 JEFFERSON DAVIS HIGHWAY, SUITE 207
ARLINGTON, VA 22202

EXAMINER	
MAIER, LEIGH C	
ART UNIT	PAPER NUMBER
1623	

DATE MAILED: 06/30/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/071,541	HUANG ET AL.	
	Examiner	Art Unit	
	Leigh C. Maier	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 April 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6 and 8-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6 and 8-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on April 18, 2005 has been entered.

Claim 7 is canceled. Claim 4 is currently amended. Any rejection or objection not expressly repeated has been withdrawn. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112 – 1st paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-6 and 8-16 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that Applicant, at the time the application was filed, had possession of the claimed invention.

The claims are drawn to a method of treatment comprising the administration of a combination of agents, wherein the agents are described in terms of their function, tyrosine kinase inhibition and therapy to induce apoptosis. A description in terms of function may be adequate when the functional characteristics are coupled with a known or disclosed with a known or disclosed correlation between function and structure or by a combination of such identifying characteristics, sufficient to demonstrate that Applicant was in possession of the claimed genus.

According to the MPEP §2163 I. A. "the issue of a lack of adequate written description may arise even for an original claim when an aspect of the claimed invention has not been described with sufficient particularity such that one skilled in the art would recognize that the applicant had possession of the claimed invention. The claimed invention as a whole may not be adequately described if the claims require an essential or critical feature which is not adequately described in the specification and which is not conventional in the art or known to one of ordinary skill in the art." The MPEP states in §2163 II 3 ii) "The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice (see i)(A), above), reduction to drawings (see i)(B), above), or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus (see i)(C), above). See *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406."

The Court of Appeals for the Federal Circuit held in *University of California v. Eli Lilly and Co.* 43 USPQ2d 1398 at 1406. "[a] written description of an invention involving a chemical genus, like a description of a chemical species, requires a precise definition, such as by structure, formula, [or] chemical name, "of the claimed subject matter sufficient to distinguish it from other materials. *In re Smythe*, 480 F.2d 1376, 1383, *Fiers* , 984 F.2d at 1171, 25 USPQ2d at 1606; *In re Smythe*, 480 F.2d 1376, 1383, 178 USPQ 279, 284-85 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus. . . .")." Applicant's functional definitions in the claimed formula simply lack the precision required by the Court of Appeals for the Federal Circuit.

According to the MPEP §2163.02 Standard for Determining Compliance With the Written Description Requirement,

> "The courts have described the essential question to be addressed in a description requirement issue in a variety of ways. An objective standard for determining compliance with the written description requirement is, "does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed". *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989). Under *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991), to satisfy the written description requirement, an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention, and that the invention, in that context, is whatever is now claimed. The test for sufficiency of support in a parent application is whether the disclosure of the application relied upon "reasonably conveys to the artisan that the inventor had possession at that time of the later claimed subject matter". *Ralston Purina Co. v. Far-Mar-Co., Inc.*, 772 F.2d 1570, 1575, 227 USPQ 177, 179 (Fed. Cir. 1985) (quoting In *re Kaslow*, 707 F.2d 1366, 1375, 217 USPQ 1089, 1096 (Fed. Cir. 1983))."

This case was filed before Applicants had a clear idea of the structures of their desired agents, other than the particular tyrphostins and chemotherapeutic agents particularly recited in the dependent claims, having the recited function or how to make those undescribed compounds. The examiner recognizes that it is not required that the patent to set forth the exact chemical structure of compounds in question, but "[i]t is only necessary that the patent set forth enough detail to allow a person of ordinary skill in the art to understand what is claimed and to recognize that the inventor invented what is claimed." See *University of Rochester v. G. D. Searle & Co.* 68 USPQ2d at 1432 (CAFC 2004). This requirement may be met by disclosing sufficiently detailed, relevant identifying characteristics when coupled with a known or disclosed *correlation between function and structure.* No such correlation has been disclosed here. Other than the particular tyrphostins and the particular mutants ΔEGFR, the specification discloses no assay for screening for such compounds or any guidance as to the possible structural elements that such agents would be likely to possess. Indeed, no screening could be described because in addition to known mutations, the scope of the claims includes mutations yet undiscovered at the time of the invention. The specification provides broad areas of future research and speculation, inviting undue experimentation in learning how to use Applicant's invention.

Applicants are reminded of what the U.S. Court of Appeals Federal Circuit wrote in *University of California v. Eli Lilly and Co.* 43 USPQ2d 1398, "In claims involving chemical materials, generic formulae usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass. Accordingly, such a formula is normally an adequate description of the claimed genus." "A definition by function, as we have previously indicated,

does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. See *Fiers*, 984 F.2d at 1169-71, 25 USPQ2d at 1605-06 (discussing Amgen). "It is only a definition of a useful result rather than a definition of what achieves that result." "The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See *In re Wilder*, 736 F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate.")".

Claims 1-6 and 8-16 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for particularly recited agents in the treatment of cells expressing ΔEFGR, does not reasonably provide enablement for the treatment of all possible EFGR mutants, known and unknown, with undescribed tyrosine kinase inhibitors and apoptosis inducing agents. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Many of the factors regarding undue experimentation have been summarized in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Circ. 1988) as follows:

(1) The quantity of experimentation necessary (time and expense);
(2) The amount of direction or guidance presented;
(3) The presence or absence of working examples of the invention;
(4) The nature of the invention;
(5) The state of the prior art;
(6) The relative skill of those in the art;
(7) The predictability or unpredictability of the art; and
(8) The breadth of the claims.

The claims are drawn to a method for modulating an apoptosis effect by the administration of a combination of a tyrosine kinase inhibitor and a therapy that is effective to induce apoptosis. Regarding the agents to be used, any method(s) for using (in a therapeutic method or inclusion in a kit) agents other than particularly recited agents are not enabled due to lack of written description. This is addressed above. Although the relative skill in the art would be fairly high, the scope of the claims is extremely broad while the amount of guidance provided is quite small. The only guidance provided by the specification is limited to the ΔEFGR mutant. Other than a wholesale screening of known compounds, there is no suggestion as to how one of ordinary skill might go about selecting additional appropriate inhibitors. There is surely no guidance as to how to prepare ones that are yet unknown. One of ordinary skill would require undue experimentation when limited to the target, ΔEFGR. The artisan would clearly require undue experimentation in order to prepare agents aiming at undiscovered targets, that is, EGFR mutants unknown at the time of the invention.

Claim Rejections - 35 USC § 102

Claims 1-4, 6, and 9-15 are rejected under 35 U.S.C. 102(b) as being anticipated by Tsai et al (Cancer Res., 1996) with Garcia de Palazzo et al (Cancer Res., 1993) or Paez et al (Science, 2004) to support inherency.

Tsai and Garcia de Palazzo teach as set forth in previous Office actions.

Paez teaches that a variety of EGFR gene mutants are expressed in NSCLC adenocarcinoma. See entire reference, particularly Fig. 1.

Applicant's arguments filed April 18, 2005 have been fully considered but they are not persuasive.

Applicant argues that there is no evidence that AG825 is relatively selective for mutant EGFR. The examiner agrees that the reference comprises no data disclosing such selectivity. However, the accompanying references support the prima facie case for the likelihood that a mutant EGFR is present, and the enhanced chemosensitivity to the chemotherapeutic agents in combination with AG825 supports the likelihood of selectivity.

Applicant contends that the examiner's previous citation of *Best* and *Fitzgerald* were incorrect applications of these cases but fails to explain the alleged deficiency. Applicant also cites *ex parte Levy*. The examiner has reviewed the case and does not find it to be on point. In that case, the examiner apparently incorrectly discounted affidavits that disputed the allegation of inherency. Applicant has produced no such evidence. It also appears that in that case a *lack* of inherency could be determined from the original reference. That is a different set of circumstances from the instant prosecution. The examiner maintains that a proper prima facie case has been made to support inherency.

Allowable Subject Matter

The unexpected results of synergism seen in the administration of a (described) tyrosine kinase inhibitor that is relatively selective for the product of ΔEGFR in combination with a (described) apoptosis inducing agent has been noted previously. A claim to that effect with proper written description would be allowable.

Examiner's hours, phone & fax numbers

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leigh Maier whose telephone number is (571) 272-0656. The examiner can normally be reached on Tuesday, Thursday, and Friday 7:00 to 3:30 (ET).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. James O. Wilson (571) 272-0661, may be contacted. The fax number for Group 1600, Art Unit 1623 is (703) 308-4556 or 305-3592.

Visit the U.S. PTO's site on the World Wide Web at http://**www.uspto.gov**. This site contains lots of valuable information including the latest PTO fees, downloadable forms, basic search capabilities and much more.

Leigh C. Maier

Leigh C. Maier
Primary Examiner
June 24, 2005